



UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/466,698	06/06/95	SANSONETTI	2356-0043-02

HM22/1013

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EXAMINER
NAVARRO, A

ART UNIT 1645 PAPER NUMBER

36

10/13/99

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☒ THE PERIOD FOR RESPONSE:

- a) ☒ is extended to run 5 months or continues to run _____ from the date of the final rejection
- b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☒ Applicant's response to the final rejection, filed 9/9/99 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☒ The proposed amendments to the claim and/or specification will not be entered and the final rejection stands because:
- a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.
 - b. ☒ They raise new issues that would require further consideration and/or search. (See Note).
 - c. ☐ They raise the issue of new matter. (See Note).
 - d. ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
 - e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See Attached

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.
3. ☒ Upon the filing an appeal, the proposed amendment ☐ will be entered ☒ will not be entered and the status of the claims will be as follows:

Claims allowed: _____
Claims objected to: _____
Claims rejected: 1-8, 10, + 13-24.

However;

☐ Applicant's response has overcome the following rejection(s): _____

4. ☐ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because _____
5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficient reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

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ADVISORY ACTION

Applicant's amendment after final filed on September 9, 1999 (Paper Number 34) has been received but not entered. Applicant's amendment has not been entered since the proposed amendment of deleting "only" from claims 1 and 13 would require a new search and consideration of the prior art, since the new claim limitation would completely exclude the use of transposon mutagenesis, while the current claim language allows for transposon mutagenesis. Consequently the amendment filed September 9, 1999 has not been entered.

Claim Rejections - 35 USC § 112

1. The rejection of claims 1-8, 10, and 13-24 under 35 U.S.C. 112, first paragraph, for reasons set forth in the Office Action mailed February 22, 1999 (Paper Number 29) is maintained.

Applicant's initially assert that Paper No. 29 appears to set forth no additional reasons for the rejection beyond those presented in Paper No. 32. Applicant's assert that if, in making this rejection, the Examiner is relying on grounds not stated in Paper No. 29 or Paper No. 32, applicant's respectfully request withdrawal of the finality of the Office Action. However, the Examiner has maintained the rejection of Paper No. 32 based on the teachings of record in response to Applicant's amendment (Paper No. 31) which amended the claims by inserting a period "." at the end of claim 17 line 3. No amendment or argument was made concerning this rejection. As stated in MPEP 706.07 "the final rejection may refer to such a statement and also should include a rebuttal of any arguments raised in the Applicant's response." Since the rejection

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was not responded to no rebuttal beyond the reasons set forth in Paper No. 29 is deemed necessary.

Applicant's are reasserting that the mutagenesis technique taught by the specification does not require knowledge of the nucleotide sequence of the target genes, does not require knowledge of regions of genes responsible for biological activity, and the number of nucleotides deleted or inserted is not critical to the practice of the claimed invention. Applicant's further assert that the method of Prentki and Krisch is not transposon mutagenesis, but an alternative to transposon mutagenesis involving an interposon. Applicant's arguments have been fully considered but are not found to be fully persuasive.

Applicant's arguments are not found to be fully persuasive in view of the teaching of Baudry *et al* (Submitted by Applicant's October 9, 1997, Paper Number 20, Exhibit 2) which set forth that "The available data indicate that the invasive ability of *S. flexerni* is a very complex phenomenon which involves many genes and a large array of polypeptides" and "Whether all these gene products are directly involved in the interaction with the cells, or whether a pool of polypeptides is necessary for transformation and/or correct positioning of a unique product is yet not known." (See page 3411). In view that Baudry *et al* set forth that the invasive ability of *S. flexerni* involves many genes, and that it is unclear whether all these gene products are directly involved in the interaction with the cells, one of skill in the art would be forced into undue experimentation to determine which genes or combination of genes, and which modifications can be made to inactivate genes is unpredictable and the experimentation left to those skilled in the art

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is unnecessarily, and improperly, extensive and undue, (Ex parte Forman 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986)). Furthermore, Applicant's assert that claim 1, recites "other than only by inactivation by means of a transposon inserted into the genes" Applicant's conclude that therefore, the quotation taken from Prentki and Krisch is not relevant to enablement of the claimed method. However, Applicant's claims recite "other than by only a transposon" consequently transposon mutagenesis is encompassed within the scope of the claims if combined with another method of mutation, (e.g. pinpoint deletion), or even multiple transposons inserted within the genes. Therefore the teachings of Prentki *et al* are relevant to the scope of the claims, Prentki lists a number of obstacles which include, "Several difficulties, however, are associated with the use of transposons mutagens. First, some transposable elements exhibit a bias for the position of integration into the target molecule, either in a sequence specific manner..., or through a strong preference for A/T rich regions... Second, transcriptional activity into adjacent DNA has been reported..., sometimes complicating the phenotypic and genetic characterization of insertion mutants. Finally, once inserted into the target molecule, transposable elements have the capacity to generate DNA rearrangements such as deletions or inversions." (See page 311) For the reasons set forth in Paper Number 32, as well as the above cited reasons this rejection is maintained.

2. The rejection of claims 13-14 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

Applicant's assert that "the broader concept that Tox-Shigella other than SC501, SC504, SC504, and SC506 could be generated by minor modification of Applicant's methods would naturally occur to the skilled artisan." Applicant's arguments have been fully considered but are not found to be fully persuasive.

Applicant's arguments are not found to be fully persuasive in view of the claim language of claim 13 which recites "wherein said *Shigella* is other than those designated SC501, SC504, SC505, and SC506." While Applicant's set forth in the specification that "various modifications" can be made in the method and vaccine" this does not provide support for claiming an entire genus of the species "*Shigella*" based on the teaching of the preferred embodiments of individual species designated SC501, SC504, SC505, and SC506. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." For reasons of record in Paper Number 32, as well as the above cited reasons, this rejection is maintained.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Dr. Anthony Caputa can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should be faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.



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October 7, 1999